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09/881,572	06/14/2001	Monica Judith Roth	601-1-095N	5861

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EXAMINER

WESSENDORF, TERESA D

ART UNIT

PAPER NUMBER

1639

DATE MAILED: 08/12/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/881,572

Applicant(s)

ROTH ET AL.

Examiner

T. D. Wessendorf

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 02 June 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-17 and 19-31 is/are pending in the application.
- 4a) Of the above claim(s) 1-14, 17, 20-25 and 27-30 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 15-17, 19, 26, 31 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

### Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

### Attachment(s)

- |                                                                                              |                                                                             |
|----------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                             | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)         | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____                                    |

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**DETAILED ACTION**

***Status of Claims***

Claims 1-17 and 19-31 are pending.

Claim 18 has been cancelled in the amendment of 6/2/03.

Claims 1-14, 17(non-elected species), 20-25 and 27-30 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

Claims 15-17(the elected species), 19, 26 and 31 are under examination.

***Claim Rejections - 35 USC § 112, first paragraph***

The following is a quotation of the first paragraph of 35

U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 15-17, 19, 26 and 31 are rejected under 35

U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for reasons advanced in the last Office action.

***Response to Arguments***

As a preliminary matter, applicants state that claim 17 has been withdrawn from consideration as being drawn to non-elected species. However, as stated above, claim 17 is withdrawn from consideration with respect to the non-elected species. It is still pending and under examination with respect to the elected species. [Note applicants should have cancelled this claim since the amended independent claim now recites the elected species].

Applicants argue that Examples 1 and 2 illustrate the screening methods of the invention by successfully identifying retroviral vectors capable of infecting novel host cell targets such as D17 canine osteosarcoma cells and human osteosarcoma cells and prostrate tumor cell lines. The specification is argued to present a description of a modification to the retrovirus env random-peptide display library useful in the identification of retroviruses capable of targeting macrophage and T-cell hosts (Example 6). Examples 1 and 2 are argued to provide significant detail that pertains to the creation of env protein libraries. The results describe FELV-A env protein introduced into the cell. Applicants note that a skilled artisan could readily analyze sequences of other retroviruses to align env proteins similar to the region of the FELV-A. Resultant

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alignment analyses may be used to delineate similar sites in different retroviruses wherein stretches of randomized residues can be incorporated so as to produce random peptide libraries in the Env proteins of other retroviruses. The present disclosure and the references cited therein as well as the general knowledge pertaining to the alignment of sequences renders the execution of such analyses well within the capability of a skilled practitioner.

In response, it is not controverted that the specification recites for specific retrovirus, Felv-A that targets specific host, as stated by applicants above. However, there is nothing in the specification or prior art teachings that indicates the extrapolation or applicability of the specific retrovirus, Felv to any other retroviruses. The statement in the disclosure at page 19, penultimate paragraph attest to this fact. It states, "although the C subgroup FelV has a broad host range, EF shows very highly specific infection of the D17 canine osteosarcoma cells". Furthermore, to applicants' REMARKS at page 7 which states that the specification is not directed to screening simply for viral attachment but involves viral infection, or more specifically, viral gene transfer, which is a far more complicated process than cellular attachment. It is well documented that binding does not necessarily lead to gene

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transfer. Thus, there is no distinguishing characteristic of the different random display viruses or the host cells that enables isolation of one infected host cell from the other. Nor is there a general method steps that can isolate one virus or infected cell from the other viruses. The Example provided in the specification, as recognized by applicants, recites for a specific virus, Felv A, not any other type of the broad Felv. This is because as applicants stipulate the Felv-A has been selected because its env receptor binding domain is a much simpler structure. Its receptor determining region **has been well characterized** and shown to consist of a short stretch of amino acids. It is apparent that the requirement or condition of a specific retrovirus as Felv A is different from even those of its own Felv family, let alone, for any or all types of different retroviruses. Battini(PNAS) discloses at page 1385, col. 1 that "although present in many copies in mouse genome, ..murine leukemia viruses cannot infect cells from laboratory mice because of the lack of a functional cell surface receptor required for virus entry." Applicants' arguments as to the alignment of the different retroviruses are lacking in the specification.

Applicants argue that guidance relating to the use of selectable markers and means for selection of cells expressing

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these markers and the techniques for selection is well known in the art. In response, the selectable markers used in the specification are specifically adapted for the retrovirus, Felv. Selectable markers are well known in the art, but the applicability of the different markers for the instant method is not clearly apparent from the disclosure.

Applicants argue that ten amino acid residues are randomized using degenerate nucleotide sequence substitutions as described in the specification with the **probability** of obtaining a stop codon of **approximately 50%**. This does not lead to an unacceptable high likelihood of premature peptide termination. A library containing two million random nucleotide sequences, for example, would still encode one million open reading frames despite a 50% frequency of stop codon termination. This frequency of premature peptide termination is experimentally viable as evidence by the success of the present inventors using this technique.

In response, while the success achieved by the present inventors relies on the specific Felv, however, it is not apparent whether this holds true for any type of retroviruses. It is not apparent from the other retroviruses whether the one million encoding open reading frames in fact represents the desired expressed retrovirus since the other half has not been

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expressed. As a skilled artisan is well aware, this incomplete expression of the product from a library is still the greatest obstacles or challenge faced in the field by skilled artisan.

Amended claim 5, step 2, is not described or supported in the as-filed specification. The as-filed specification does not describe a method comprising of the presently claimed step 2. Applicants rely on page 3, lines 10-16, page 19, lines 1-2 and page 11, lines 10-12 as describing the amended claim 5. None of these cited sections provide a description or support for the now added step 2. This step is repetitive of the step recited in step 1 except for the terminology used i.e., inoculating, instead of administering.

***Claim Rejections - 35 USC § 112, second paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Amended claims 15-17, 19, 26 and 31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 15 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential



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steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the steps of identifying a retrovirus from the host cells. It is not clear as to how the identifying step is done from the inoculated host cells. Furthermore, step 2 appears to be redundant as it is the same as step 1 differing only in the terms administering and inoculating. (The specification does not recite a method with the newly incorporated step 2). Claim 15 is unclear as to the method of administering a random peptide library i.e., how administration is done to a host cell, in the context of the claim.

B. Claim 16 is indefinite in reciting that each virus of the plurality encodes an env protein of the virus. A virus does not encode a protein. Also, "on the same nucleic acid molecule" lacks antecedent support from the base claim.

C. Claim 26 is confusing as to how a retrovirus is identified. The base claim does not recite any identifying step except reciting the term identifying.

D. Claim 31 is indefinite for the reasons given in paragraph A, above. The metes and bounds of "divergent" amino acid sequence are not clearly circumscribed by the claim.

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E. Claim 17 does not further limit the base claim and broadens the base claim with the recitation of the other viruses.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 15-17, 19, 26 and 31 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Buchholz (Nature Biotechnology).

**Response to Arguments**

Applicants admit that the Buchholz et al reference is directed to the incorporation of random peptides into the N-terminus of the Env protein. But argue that Buchholz does not suggest a method wherein random peptide sequences are incorporated into a receptor binding domain of the env protein or teach that such a method could be used to generate mutated retroviral particles having altered host specificity. Attention is directed to page 951, cols. 1 and 2, and Fig. 1 at page 952. Buchholz discloses a method in which the random peptide is inserted at the N-terminal of the soluble unit of the envelope protein which is known as the receptor binding specificities of the particles. [Note applicants' disclosure at page 11, fourth complete paragraph of the disclosure which states that ".....extensive analyses have localized the receptor binding domain to the N-terminal half of the SU protein....."]

It is considered that the soluble units (SU) of the envelope protein would inherently or if not, obviously would be the variable regions of the envelope (as in claim 31) to which binding occurs. Variation of amino acids in a protein, as the inserted random peptide, is normally done on the variable regions of a protein.

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In view of the amendments to the claims, the 35 USC 102 rejection over Russell and the 103 rejection over the combined teachings of Russell or Buchholz in view of Larocca are withdrawn.

No claims are allowed.

### **Conclusion**

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

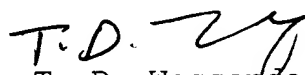
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This application contains claims 1-14, 17(non-elected species), 20-25 and 27-30 drawn to a nonelected invention. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is (703) 308-3967. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (703) 306-3217. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-7924 for regular communications and (703) 308-7924 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

  
T. D. Wessendorf  
Primary Examiner  
Art Unit 1639

tdw  
August 7, 2003